The invention provides isolated nucleic acid and amino acid sequences of hKir5.1, antibodies to hKir5.1, methods of detecting hKir5.1, methods of screening for inward rectifier potassium channel activators and inhibitors using biologically active hKir5.1, and kits for screening for activators and inhibitors of inward rectifier potassium channels comprising hKir5.1.--

REMARKS

I. Status of the Application

Claims 1-35 were originally filed. Claims 1-4 and 6-7 pending and are currently under examination.

Claim 1 has been amended to recite specific hybridization conditions, which find support in the specification, *e.g.*, on page 21 lines 11-13 and lines 18-20. Claim 6 as amended uses the word "predicted" to describe how molecular weight is determined, support for which is found, *e.g.*, on page 8 lines 3-5. No new matter is introduced.

Further, the present amendment reinstates the omitted abstract of the disclosure, which was contained in the provisional application and the PCT application. No new matter is introduced.

II. Information Disclosure Statement

The Examiner informed Applicants the failure to comply with 37 CFR §1.98(a)(2) in association with the filing of the information disclosure statement in August 2001. Applicants hereby submit a supplemental information disclosure statement with copies of the two Genbank entries.

III. Objections

A. Updated Status of the Parent Non-provisional Application

The Examiner objected to the application for lack of updated status of the parent non-provisional application. The present amendment has addressed the issue.

B. Embedded Hyperlink

The Examiner also objected to the application for containing hyperlink and/or other forms of browser-executable code. The present amendment has deleted the hyperlink embedded in the text.

C. Title of the Invention

The Examiner further objected to the title of the application for not being descriptive. The title has been amended according to the Examiner's suggestion.

IV. Claim Rejections

A. 35 USC §101

The Examiner rejected claims 1-9 under 35 USC §101 for alleged lack of either a credible, specific, and substantial asserted utility or a well established utility. Applicants respectfully traverse the rejection.

The present invention, the identification of the Kir5.1 channel, has a specific, substantial and credible utility. The identification of nucleic acids encoding the Kir5.1 channel has utility because it makes possible the routine identification of agonists

and antagonists of the Kir5.1 channel, *e.g.*, for the treatment of diseases related to cell excitability.

Introduction

In order to assess utility, the Examiner should review the specification to determine if there are any statements asserting that the claimed invention is useful for any particular purpose. An invention has utility if the utility is specific, substantial, and credible, or a utility that is well established. A utility is specific if it is specific to the subject matter claimed. A utility is substantial if it has a real-world use. A utility is credible if it would be believable to one of skill in the art. In most cases, an applicant's assertion of utility creates a presumption of utility that is sufficient to satisfy the utility requirement of 35 USC § 101.

A *prima facie* showing of lack of utility by the Examiner must establish that it is more likely than not that a person of ordinary skill in the art would not consider that any utility asserted by the applicant would be specific and substantial. The present application claims nucleic acids that encode Kir5.1 ion channels. After reading the application, the skilled practitioner would appreciate that Kir5.1 ion channels are involved in maintaining the resting potential and in controlling excitability of a cell. Thus, the ion channel can be used to as a target for treating disorders related to relevant cell excitability, *e.g.*, hypertension, acute renal failure, chronic renal failure, diabetes insipidus, diabetic nephropathy, hypothyroidism, hyperthyroidism, goiter, hypoparathyroidism, hyperparathyroidism, pancreatic insufficiency, diabetes, cystic fibrosis, sialorrhea, and salivary insufficiency, as described on page 6, lines 28-31, page 9, lines 19-24, and page 58, lines 15-21 of the present patent application.

In addition, the skilled practitioner would (1) know how to routinely identify agonists or antagonists of Kir5.1 channels using the claimed nucleic acids sequences and the disclosed methods for activation of Kir5.1 channels, and (2) understand that antagonists or agonists of Kir5.1 channels are useful, *e.g.*, for modulating

cell resting potential and in controlling diseases related to cell excitability, as listed above. The Applicant, therefore, submits that the claimed nucleic acids have a specific, substantial and credible utility.

The Kir5.1 channel is an inward rectifying potassium channel that modulates cell excitability and resting potential

In the present Office Action, the Examiner does not dispute Applicant's assertion that the claimed nucleic acids encode a new potassium channel. The Examiner disputes Applicant's assertion that the new potassium channel, Kir5.1, has a practical utility. The Applicant respectfully traverses. The Applicant respectfully traverses because the Examiner provides no reasons why one of skill in the art, after reading the present specification, would not believe the Kir5.1 channel to be an inward rectifying potassium channel useful for modulating cell excitability and membrane potential.

The Kir5.1 channel is a widely expressed inward rectifying potassium channel. It is well known in the art that inward rectifying potassium channels play key roles in the modulation of neuronal, and therefore, cell excitability (*see, e.g.*, Nichols & Lopatin, *Ann. Rev. Physiol.* 59:171-191 (1997)). In Example 1 of the specification, the Applicant expressed human Kir5.1 according to standard methodology in cells and demonstrated that the claimed nucleic acids encode an inward rectifying potassium channel (*see* page 57 and Figure 1 of the specification). Figure 2 of the present specification demonstrates that Kir5.1 is widely expressed in different cell types. Accordingly, the Applicant submits that the claimed nucleic acids encode an inwardly rectifying potassium channel useful for modulating cell excitability. Because the Kir5.1 channel is capable of modulating cell excitability, the Kir5.1 channel is a useful target for the treatment of diseases and conditions caused by altered neuronal and cell excitability, *e.g.*, hypertension, acute renal failure, chronic renal failure, diabetes insipidus, diabetic nephropathy, hypothyroidism, hyperthyroidism, goiter, hypoparathyroidism,

hyperparathyroidism, pancreatic insufficiency, diabetes, cystic fibrosis, sialorrhea, and salivary insufficiency.

After reading the present application, the skilled practitioner would know how to identify Kir5.1 channel agonists and antagonists useful for modulating cell excitability

It is well known in the art that once an ion channel has been identified, agonists or antagonists of the ion channels can be routinely identified using the coding sequence of the ion channel gene and a method for activation of the channel. The present application provides sequences encoding a Kir5.1 channel. The present application also provides methods for modulating a Kir5.1 channel. Agonists and antagonists of Kir5.1 can routinely be identified by applying compounds to Kir5.1-expressing cells. After reading the present application, the skilled practitioner, therefore, would know how to identify Kir5.1 channel agonists and antagonists useful for modulating cell excitability.

The identification of the Kir5. channel is useful (1) for modulating cell excitability (2) for identifying Kir5.1 channel agonists or antagonists capable of modulating Kir5.1 channels, and (3) as a target for treating diseases

There are many instances where modulation of an ion channel is useful for treating a specific disease even though the channel itself may not cause disease. For example, hypertension can be caused by a variety of illnesses such as renal disease and diabetes. Among common treatment strategies for hypertension is the use of drugs such as calcium channel blockers to relax the vasculature. Relaxing the vasculature to reduce blood pressure is useful and effective, even if the original cause of the hypertension is unrelated to vascular tone. Similarly, it is perfectly reasonable to expect that the targeting of Kir5.1, a widely expressed inwardly rectifying potassium channel, is an appropriate strategy for modulating cell excitability and resting potential without respect to the original cause of the condition.

The demonstration that Kir5.1 channels are functional inwardly rectifying channels, coupled with the methods of modulating Kir5.1 channels provided in the specification and the level of skill in the art of ion channels, is sufficient to demonstrate specific, substantial, and credible utility

The Applicant maintains that the demonstration that the Kir5.1 channel is a functional inwardly rectifying potassium channel, coupled with the methods disclosed in the specification and the level of skill in the art of ion channels, is sufficient to demonstrate specific, substantial and credible utility.

Specific utility

The Applicant asserts that the present invention has a specific utility. Specific utility is defined by the MPEP as a utility that is specific to the subject matter claimed. The MPEP explains that applications show sufficient specific utility when applicants disclose a "specific biological activity" and reasonably correlate that activity to a "disease condition." MPEP 2107.01, 2107.02. In this application, The Applicant discloses a "disease condition", cell excitability and resting potential, that correlates with a "biological activity", the opening and closing of Kir5.1 channels. This application demonstrates that Kir5.1 channels modulate cell excitability. This application provides methods of identifying agonists and antagonists of Kir5.1 channels capable of modulating Kir5.1 channels e.g., for the treatment of diseases as listed above. The Applicant therefore submits that the present invention has a specific utility, e.g., identification of Kir5.1 channels that influence cell excitability and methods of using the claimed invention to identify agonists or antagonists of kir5.1, e.g., useful for treating diseases of cellular excitability.

Substantial utility

The Applicant also asserts that the present invention has a substantial or "real world" use. This invention provides nucleic acids that encode Kir5.1 channels. The

application also demonstrates that Kir5.1 channels modulate cell excitability. This application therefore has real world use in the modulation of cell excitability and in the identification of compounds that modulate the Kir5.1 channel. As previously discussed, it is well known in the art that once an ion channel has been identified, agonists or antagonists of the ion channels can be routinely identified using the coding sequence of the ion channel gene and a method for activation of the channel. Throughout the specification, the Applicant teaches how to activate the Kir5.1 channel and how to identify agonists and antagonists of the Kir5.1 channel. For example, on page 40 of the specification to page 44, the Applicant provides assays that can be used to test for inhibitors and activators of the Kir5.1 channel, e.g., assays that involve measuring current, measuring membrane potential, measuring ion flux, or measuring patch-clamp electrophysiology. The Applicant therefore submits that the present invention has a substantial utility, e.g., the identification of Kir5.1 channels that modulate cell excitability, thereby making routine the identification of agonists or antagonists of Kir5.1 channels useful for treating diseases of cellular excitability.

Credible utility

Finally, The Applicant asserts that the present invention has a credible utility. According to the MPEP, when an applicant has specifically asserted that an invention has a particular utility, that assertion cannot simply be dismissed by Office Personnel as being "wrong," even when there is reason to believe that the assertion is not entirely accurate. Rather Office Personnel must determine if the assertion of utility is credible, (i.e., whether the assertion of utility is believable to a person of ordinary skill in the art based on the totality of the evidence and reasoning provided) MPEP 2107.02 III B. The Applicant submits that one of skill in the art after reading this application would (a) know how to identify Kir5.1 channels (b) know how to identify agonists or antagonists of Kir5.1 channels (c) know how to use those agonists or antagonists to modulate cell excitability. Because many currently marketed drugs treat diseases of excitability, e.g.,

epilepsy, by targeting ion channels, the skilled practitioner would believe that the identification of a new inwardly rectifying potassium channel and methods of identifying agonists and antagonists of the newly identified channel are useful.

Accordingly, The Applicant respectfully requests that the utility rejection under 35 U.S.C. § 101 be withdrawn.

B. 35 USC §112 First Paragraph

Enablement Rejections

Claims 1-9 were rejected under 35 USC §112 first paragraph. According to the Examiner, since the application fails to provide a real world utility for the invention, one skilled in the art will not know how to use the invention, the invention thus necessarily fails the enablement test. In light of the forgoing discussion, Applicants submit a real world utility is established and the enablement rejections associated with lack of utility are traversed.

The Examiner further stated that even if a patentable utility was shown, the disclosure was not fully enabling for the scope of the pending claims 1-7 and 9. Applicants respectfully traverse the rejections.

A claimed invention is enabled when the disclosure allows one of ordinary skill in the art to make and use the invention without undue experimentation. MPEP §2164.01. The test for enablement is set forth in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). The consideration of multiple factors is necessary: the breadth of the claims; the nature of the invention; the state of the prior art; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In the present case, the claims are directed to a nucleic acid encoding a polypeptide monomer comprising an alpha subunit of a potassium channel, and the polypeptide monomer has a well-defined structure and readily testable functional feature. Working examples of human Kir5.1 coding sequence and amino acid sequence are provided. The specification also contains ample directions to practice the invention, such as methods of cloning human Kir5.1 nucleic acid sequences (*see, e.g.*, page 24 line 29 to page 26 line 29 and Example I), expression of hKir5.1 nucleic acid sequences (*see, e.g.*, page 27 line 2 to page 29 line 15), purifications of hKir5.1 polypeptides (*see, e.g.*, page 29 line 18 to page 32 line 17), immunological detection of hKir5.1 polypeptides (*see, e.g.*, page 32 line 20 to page 39 line 29), and assays for activity of an inward rectifier potassium channel and modulators of hKir5.1 (*see, e.g.*, page 40 line 2 to page 44 line 20 and Example II). The level of technical sophistication is high in the art, and Kir5.1 inward rectifier potassium channel variants can be readily tested according to the methods commonly used by those skilled in the art or the methods taught by the specification (such as nucleic acid or amino acid sequence comparison, nucleic acid hybridization assays, and assays for potassium channels with the inward rectifier characteristics) to eliminate inoperable embodiments. MPEP §2164.01 states, complex experimentation is not necessarily undue, if the art typically engages in such experimentation. In the present case, although some experimentation may be involved to practice the invention using embodiments other than those specifically described in the application, such experimentation utilizes well-established techniques and is routinely conducted in the art. Thus, the experimentation does not constitute undue experimentation.

In rejecting claims 1-7 and 9 for alleged lack of enablement, the Examiner expressed the concerns over functional predictions of a protein based on its sequence homology to another protein with known functions. Applicants agree with the Examiner in that such predictions are unreliable in many instances. Yet, Applicants respectfully

note that such unreliability is irrelevant to the enablement of the claimed invention in the present case, because the claimed genus of nucleic acids must satisfy **both** the structural element (encoded by a nucleic acid that hybridizes under stringent conditions to a reference nucleic acid) and the functional element (encoding a polypeptide monomer capable of forming, with at least one additional Kir alpha subunit, an inward rectifier potassium channel). The determination of functional element of the claimed nucleic acids is independent of the structural element. As discussed in the last section, the specification teaches the methods for assessing the activity of an inward rectifier potassium channel (*see, e.g.*, page 40 lines 3-9 and Example II), which do not rely on amino acid sequence homology.

In summary, Applicants believe that the disclosure by the present application is sufficiently enabling for a person with ordinary skill in the art to practice the invention and that no undue experimentation is required. The rejections for inadequate enablement should thus be properly withdrawn.

Written Description Rejections

In addition, claims 1-7 and 9 were rejected under 35 USC §112 first paragraph for alleged inadequate written description. Applicants respectfully traverse the rejections.

The pending claims as amended fully comply with the requirements for written description of a chemical genus as set forth in *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997). As described by the Federal Circuit in *Lilly*, "[a] description of a genus of cDNAs may be achieved by means of . . . a recitation of structural features common to the members of the genus . . . ." *Lilly*, 43 USPQ2d at 1406. Furthermore, the court in *Fiers v. Revel* stated that an adequate written description "requires a precise definition, such as by structure, formula, chemical name, or physical properties." *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Finally, the MPEP states that structural formulas provide a convenient method of demonstrating possession

of specific molecules, MPEP 2163. The claims set forth both functional elements as well as structural elements, i.e., hybridization conditions and reference sequences to which members of the claimed genus hybridize. Therefore, the claimed sequences are thereby defined via shared physical and structural properties.

With regard to the claimed nucleic acids, the claims set forth both functional elements (*e.g.*, encoding a polypeptide, which can form an inward rectifier potassium channel with at least one additional Kir alpha subunit), as well as structural elements (*e.g.*, encoded by a nucleic acid that hybridizes to a reference sequence under specified hybridization conditions). Applicants submit, therefore, that the claimed nucleic acids are thereby defined via shared functional and structural properties.

The ability of a particular nucleic acid to hybridize under *given conditions* to a reference nucleic acid is a physical/structural property of the nucleic acid, because it relies upon the nucleotide sequence of the molecule (*see, e.g.*, Sambrook, *Molecular Cloning: A Laboratory Manual*, pp. 9.47-9.51 (2nd ed. 1989); *see also* Stryer, *Biochemistry*, pp. 573 (2nd ed. 1975)). As described in Stryer, the transition between hybridization and melting of complementary nucleic acid strands is abrupt and largely sequence dependent. When the temperature of hybridization is provided, one of skill in the art would be able to predict whether or not a given sequence would hybridize to a reference sequence (*see, e.g.*, equations provided in Sambrook, *supra*). Moreover, in the same light, the percent identity of a nucleic acid to a reference sequence is a structural feature, as it relies entirely on the sequence of the molecule.

The functional features of the claimed nucleic acids are also provided: they each encodes a polypeptide monomer, which can form an inward rectifier potassium channels with at least one additional Kir alpha subunit. As required by the standard set forth in *University of California v. Eli Lilly,* these features are common to all members of the claimed genus. The claimed nucleic acids are thus appropriately described by their structural/physical features in addition to their functional characteristics, as required by the court in *University of California v. Eli Lilly* and MPEP 2163.

The Examiner relied on *Fiddes v. Baird*, 30 USPQ2d 1481 (U.S. Patent and Trademark Office Board of Patent Appeals and Interferences, 1993), to conclude that the instant disclosure lacks sufficient written description. The Board ruled in *Fiddes* that adequate written description was not present to support a broad claim drawn to mammalian fibroblast growth factors (FGF) when only bovine pituitary FGF amino acid sequence and its theoretical nucleotide sequences were disclosed. Examiner apparently was of the opinion that the facts in *Fiddes* are analogous to that in the present case, such that a finding of inadequate written description in the present application is warranted. Applicants respectfully disagree with the Examiner's reading of the *Fiddes* case and application of *Fiddes* in the present application.

First, *Fiddes v. Baird* is not inconsistent with the standards for written description as set forth by *Lilly* or *Fiers*. In fact, the Board in *Fiddes* quoted *Fiers* in the discussion of what constitutes adequate written description. 30 USPQ2d at 1483. Moreover, the *Lilly* decision was handed down later in time than *Fiddes* (1997 v. 1993) and by a higher legal authority (Fed. Cir. v. the Board). Thus, even if any inconsistency existed, the *Lilly* decision would tramp *Fiddes*.

Second, the fact pattern of *Fiddes* is not analogous to that of the present case. In *Fiddes*, a broad claim was drawn to mammalian FGF based on the specification disclosing a bovine FGF amino acid sequence and a ***deduced*** nucleotide sequence, but not any naturally occurring FGF nucleotide sequence. As it later turned out, the deduced nucleotide sequence disclosed in the specification is significantly different from the naturally occurring FGF nucleotide sequence, largely due to codon degeneracy. In essence, the patent applicants in *Fiddes* sought to patent a large genus of polypeptide and polynucleotides when they did not have in their possession any correct polynucleotide sequence. The Board's finding of inadequate written description was based on the notion that the claim of a genus of polynucleotides cannot be adequately supported when only an ***inaccurate*** polynucleotide sequence was disclosed. The Board in *Fiddes* did not take the

position that the claim of a genus cannot be adequately supported by the disclosure of an ***accurate*** polynucleotide sequence. Nor could the Board, under *Lilly*, properly require the claim of a genus to be supported by the patent applicant's possession of every embodiment of the genus.

In contrast to *Fiddes*, Applicants of the present application have in their possession both the amino acid sequence of at least one Kir polypeptide monomer and the naturally occurring nucleotide sequence encoding the nomomer in full length (SEQ ID NOs: 1 and 2). In addition, the claims in the present application are not drawn to a broad genus of molecules without specific structural or functional definition (such as mammalian Kir polypeptide monomers). As discussed above, both structural and functional features commonly shared by the claimed genus have been described in detail, which "clearly allow persons of ordinary skill in the art to recognize that [the applicant] invented what is claimed." *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991).

Taken together, the disclosure by the present application provides both the structural/physical features and functional characteristics of the claimed genus of nucleic acids, fully satisfying the written description requirement under *Lilly* and *Fiers*. On the other hand, there exists crucial factual distinction between the present case and *Fiddes v. Baird*, which would make it improper to apply *Fiddes* mechanically. As such, Applicants respectfully request that the Examiner withdraw the rejections.

C. 35 USC §112 Second Paragraph

The Examiner further rejected claims 5, 6, 8, and 9 under 35 USC §112 second paragraph for allegedly being indefinite. Specifically, the Examiner alleged that claim 6 is vague and indefinite for omitting the method by which the molecular weight is calculated. As amended, claim 6 recites "predicted molecular weight," which one of ordinary skill in the art will understand as the molecular weight based on a polypeptide's

amino acid sequence, particularly in the context of its disclosure. See page 8 lines 3-5 of the specification (the nucleotide sequence of hKir5.1 (SEQ ID NO:2) encodes a polypeptide monomer of approximately 384 amino acids with a predicted molecular weight of approximately 43 kDa (SEQ ID NO:1) and a predicted range of 38-34 kDa). Thus, Applicants submit the indefiniteness rejection should be properly withdrawn.

Moreover, the Examiner alleged that without reciting specific hybridization conditions, claims 5, 8, and 9 fail to define the metes and bounds of the invention. The present amendment to claim 1 adds the recitation of specific hybridization conditions for both "stringent" and "moderately stringent" hybridization conditions. The indefiniteness rejections are thus properly overcome.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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APPENDIX A
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

In the paragraph under the subtitle "CROSS REFERENCE TO RELATED APPLICATIONS":

This application is a 371 of PCT/US99/04549, filed March 2, 1999, and claims priority from USSN 60/076,621, filed March 3, 1998, now abandoned, herein incorporated by reference in its entirety.

In the paragraph starting on page 19 line 14 and ending on page 20 line 2:

-- Another example of algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information [(http://www.ncbi.nlm.nih.gov/)]. This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The

BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.--

IN THE CLAIMS:

1. (Once amended) An isolated nucleic acid encoding a polypeptide monomer comprising an alpha subunit of a potassium channel, the polypeptide monomer:

(i) forming, with at least one additional Kir alpha subunit, a potassium channel having the characteristic of inward rectification; and

(ii) encoded by a nucleic acid that selectively hybridizes under highly stringent hybridization conditions to a nucleotide sequence of SEQ ID NO:2, wherein the stringent conditions comprise incubation at 42°C in a solution comprising 50% formamide, 5 x SSC, and 1% SDS or an incubation at 65°C in a solution comprising 5 x SSC and 1% SDS at 65°C with a wash in 0.2 x SSC and 0.1% SDS [having a monomer tail region that has greater than 80% amino acid sequence identity to a human Kir5.1 tail region; and

(iii) specifically binding to polyclonal antibodies generated against SEQ ID NO:1].

6. (Once Amended) The isolated nucleic acid of claim 1, wherein the nucleic acid encodes a polypeptide monomer having a molecular weight of about between 38 kDa to 48 kDa, wherein the molecular weight is predicted based on amino acid sequence.

IN THE ABSTRACT:

Following the sequence listing ending on page 65:

-- **NUCLEIC ACID ENCODING HUMAN KIR5.1**

ABSTRACT OF THE DISCLOSURE

The invention provides isolated nucleic acid and amino acid sequences of hKir5.1, antibodies to hKir5.1, methods of detecting hKir5.1, methods of screening for inward rectifier potassium channel activators and inhibitors using biologically active hKir5.1, and kits for screening for activators and inhibitors of inward rectifier potassium channels comprising hKir5.1.--